From: **Robert Helverson/R3/USEPA/US**
Sent: 3/12/2012 9:24:57 AM

To: Lora Werner/R3/USEPA/US@EPA; Dennis Carney/R3/USEPA/US@EPA
CC: Karl Markiewicz/R3/USEPA/US@EPA
Subject: Fw: Dimock /info on lithium tox and health effects

Dennis, It is included in email below.

Robert H. Helverson
Regional Representative
Agency for Toxic Substances and Disease Registry (ATSDR), Region 3
Department of Health and Human Services
1650 Arch Street (3HS00)
Philadelphia, PA 19103
(215) 814-3139 (Office)
(215) 814-3003 (Fax)

----- Forwarded by Robert Helverson/R3/USEPA/US on 03/12/2012 09:24 AM -----

From: Lora Werner/R3/USEPA/US
To: Richard Fetzer/R3/USEPA/US@EPA, Kelley Chase/R3/USEPA/US@EPA
Cc: Dawn Ioven/R3/USEPA/US@EPA, Robert Helverson/R3/USEPA/US@EPA, Karl Markiewicz/R3/USEPA/US@EPA
Date: 03/09/2012 03:36 PM
Subject: Dimock /info on lithium tox and health effects

Hi Rich and Kelley

Here is the additional info on lithium tox and health effects that you asked for from us and Dawn! We will use this to speak from whenever all the fun meetings on this start.

Happy friday, Lora

Lora Siegmann Werner, MPH
Senior Regional Representative
Agency for Toxic Substances and Disease Registry (ATSDR), Region 3
Department of Health and Human Services
1650 Arch Street, 3HS00, Philadelphia, PA 19103
phone: 215-814-3141, fax: 215-814-3003
cell: 215-588-9778
email: lkw9@cdc.gov

CDC.gov is Your Online Source for Credible Health Information. Visit
www.cdc.gov.
----- Forwarded by Lora Werner/R3/USEPA/US on 03/09/2012 03:34 PM -----

From: Dawn Ioven/R3/USEPA/US
To: Lora Werner/R3/USEPA/US
Cc: Robert Helverson/R3/USEPA/US@EPA
Date: 03/09/2012 01:38 PM
Subject: Re: Lithium language -see what you think!!

Looks good, Lora. Thanks for pulling this together so quickly. This tox summary for lithium should satisfy Rich's immediate needs; if, down the line, he wants a basic fact sheet that could be shared with the community, we could easily extract points from what you've already written. Thank you again.

Dawn

Dawn A. Ioven, toxicologist
U.S. EPA - Region III
(3HS41)
1650 Arch street
Philadelphia, PA 19103
215.814.3320

Lithium:
EPA's regional screening level (RSL) for lithium in drinking water is 31 ug/L, and PADEP's medium-specific concentration (MSC) for lithium in drinking water is 73 µg/L. EPA has derived a provisional lithium reference dose (RfD) of 0.002 mg/kg-day. This provisional reference dose is based on a Lowest Observable Adverse Effect Level (LOAEL) of 2.1 mg/kg-day for adverse effects in several organs and systems. EPA applied an uncertainty factor of 1000 in determining the RfD, which includes a factor of 10 to extrapolate from a LOAEL to a NOAEL, a factor of 10 to protect susceptible individuals and a factor of 10 to account for database insufficiencies (EPA 2008). Using this provisional RfD, screening value concentrations in drinking water can be calculated as 70 ug/L (for adults weighing 70 kg drinking 2 L/day), 20 ug/L for a 10 kg infant/child drinking 1 L/day, and 32 ug/L for a 16 kg child drinking 1 L/day.

A wide range of estimates for daily dietary intake of lithium have been reported. Some authors report estimates for the average daily dietary intake of lithium ranging from 0.24 to 1.5 µg/kg-day, while another reports an average daily dietary intake range of up to 33 to 80 µg Li/kg-day (EPA 2008).

Based on the maximum level of lithium detected in first 11 Dimock wells (236 ug/L), an adult exposure dose can be calculated of .00674 mg/kg/day and a daily intakes of 0.472 mg lithium/day. For a 10 kg child, the lithium exposure dose at 236 ug/L is 0.0236 mg/kg/day with daily intake of 0.236 mg lithium/day. For a 16 kg child, the lithium exposure dose at 236 ug/L is 0.0148 mg/kg/day with daily intake of 0.236 mg lithium/day. Therapeutically, lithium (lithium carbonate) is used to control manic episodes in manic-depressive illness in doses of 900 - 1,800 mg/day. Therefore, the estimated lithium intakes at the maximum concentrations at this site are well below reported therapeutic levels.

There is a great deal of uncertainty regarding the public health significance of environmental exposures to sub-therapeutic doses of lithium. Numerous pharmacokinetic studies of lithium have reported large inter-individual variability in response to lithium administration. Lithium treatment is not recommended for patients with significant renal or cardiovascular disease, severe debilitation or dehydration or sodium depletion or for patients receiving certain other medications (e.g., diuretics) because the risk of lithium toxicity is very high in such patients. In general, lithium demonstrates a narrow therapeutic-toxic ratio and can induce adverse health effects, if slight changes in dosing or elimination occur. There are several groups of drugs that interact with lithium causing increased levels of lithium in the serum. These include diuretics (e.g., Hydrodiuril), nonsteroidal anti-inflammatory agents (e.g., Motrin), calcium channel blocking agents (e.g., Calan), and angiotensin-converting enzyme inhibitors (e.g., Capoten). The concurrent use of any drug associated with the aforementioned groups would increase the likelihood of toxic manifestations (PADOH 1994).

Some of the signs of lithium toxicity include diarrhea, vomiting, tremors, mild ataxia, drowsiness, or muscular weakness. Thyroid impairments have been observed in individuals receiving lithium therapy (Grandjean and Aubry 2009; Lazarus 2009), and possible thyroid effects from lithium in drinking water have been reported (Broberg et al. 2011). There is sufficient evidence available to conclude that therapeutic use of lithium causes developmental effects in offspring when maternal serum lithium concentrations are within the therapeutic range (EPA 2008).

Using the maximum concentration of lithium (236 ug/L) detected in HW06, the ingestion exposure exceeds EPA's provisional chronic RfD for children and adults.

Given the safety factors employed in developing the provisional RfD, ATSDR concludes that exposure to lithium at the level detected in HW06 (and HW24 at 201-204 ug/L) is not likely to cause adverse health effects to the general population. However, this maximum drinking water concentration would be of health concern for any individuals receiving lithium therapy, and there remains uncertainty regarding the potential for health effects of elevated but sub-therapeutic doses of lithium, particularly for sensitive subpopulations (e.g., children, pregnant women, people with significant cardiovascular disease, sodium depletion, and people on medications previously discussed).

References

U.S. Environmental Protection Agency (EPA). 2008. Provisional Peer Reviewed Toxicity Values for Lithium. Superfund Health Risk Technical Support Center, National Center for Environmental Assessment, Office of Research and Development. Online at http://hhpprtv.ornl.gov/issue_papers/Lithium.pdf

Grandjean EM, Aubry JM. 2009. Lithium: updated human knowledge using an evidence-based approach: part III: clinical safety. CNS Drugs 23:397–418.

Broberg K, Concha G, Engström K, Lindvall M, Grandér M, and Vahter M. 2011. Lithium in Drinking Water and Thyroid Function. Environ Health Perspect 119:827–830.

Pennsylvania Department of Health (PADOH) 1994. Preliminary Public Health Assessment for Foote Mineral Company, Frazer, Chester County, PA.
http://www.atsdr.cdc.gov/HAC/pha/pha.asp?docid=309&pg=3

Lora Siegmann Werner, MPH
Senior Regional Representative
Agency for Toxic Substances and Disease Registry (ATSDR), Region 3
Department of Health and Human Services
1650 Arch Street, 3HS00, Philadelphia, PA 19103
phone: 215-814-3141, fax: 215-814-3003
cell: 215-588-9778
email: lkw9@cdc.gov

CDC.gov is Your Online Source for Credible Health Information. Visit www.cdc.gov.